

was then added to the succinate. In another separate flask, TPP (1.30 mmol, 338 mg) was dissolved in acetonitrile (11.7 mL) under argon. This mixture was then added to the succinate/DMAP/dTNP reaction mixture. Finally, 10.46 g pre-acid washed LCA CPG (loading = 115.2 $\mu\text{mol/g}$) were added to the main reaction mixture, vortexed shortly and placed on shaker for approximately 2 hours. A portion was removed from shaker after 2 hours and the loading was checked. A small sample of CPG was washed with copious amounts of acetonitrile, dichloromethane, and then with ether. The initial loading was found to be 46 $\mu\text{mol/g}$. (3.4 mg of CPG were cleaved with trichloroacetic acid). The absorption of released trityl cation was read at 503 nm on a spectrophotometer to determine the loading. The whole CPG sample was then washed as described above and dried under P_2O_5 overnight in vacuum oven. The following day, the CPG was capped with 25 mL CAP A (tetrahydrofuran/acetic anhydride) and 25 mL CAP B (tetrahydrofuran/pyridine/1-methyl imidazole) for approximately 3 hours on a shaker. The material was filtered and washed with dichloromethane and ether. The CPG was dried under P_2O_5 overnight in vacuum oven. After drying, 10.77 g of CPG was isolated with a final loading of 63 $\mu\text{mol/g}$.

EXAMPLE 13

5'-O-DMT- 3'-O-methoxyethyl-N⁶-benzoyl-adenosine-2'-O-succinate

[0148] 5'-O-DMT-3'-O-(2-methoxyethyl)-N⁶-benzoyl adenosine was first succinylated on the 2'-position. 3.0 g (4.09 mmol) of the adenosine nucleoside were reacted with 10.2 mL dichloroethane, 615 mg (6.14 mmol) succinic anhydride, 570 μL (4.09 mmol) triethylamine, and 251

mg (2.05 mmol) 4-dimethylaminopyridine. The reactants were vortexed until dissolved and placed in heating block at 55 °C for approximately 30 minutes. Completeness of reaction was checked by thin layer chromatography (TLC). The reaction mixture was washed three times with cold 10% citric acid followed by three washes with water. The organic phase was removed and dried under sodium sulfate. Succinylated nucleoside was dried under P₂O₅ overnight in vacuum oven.

EXAMPLE 14

5'-O-DMT- 3'-O-(2-methoxyethyl)-N⁶-benzoyl-adenosine-2'-O-succinoyl Linked LCA CPG

[0149] Following succinylation, 5'-O-DMT-3'-O-(2-methoxyethyl)-2'-O-succinyl-N⁶-benzoyl adenosine was coupled to controlled pore glass (CPG). 3.41 g (4.10 mmol) of the succinate were dried overnight in a vacuum oven along with 4-dimethylaminopyridine (DMAP), 2,2'-dithiobis (5-nitro-pyridine) (dTNP), triphenylphosphine (TPP), and pre-acid washed CPG (controlled pore glass). The following day, DMAP (4.10 mmol, 501 mg) and acetonitrile (37 mL) were added to the succinate. The mixture was "mixed" by a magnetic stirrer under argon. In a separate flask, dTNP (4.10 mmol, 1.27g) was dissolved in acetonitrile (26 mL) and dichloromethane (11 mL) under argon. This reaction mixture was then added to the succinate. In another separate flask, TPP (4.10 mmol, 1.08 g) was dissolved in acetonitrile (37 mL) under argon. This mixture was then added to the succinate/DMAP/dTNP reaction mixture. Finally, 33 g pre-acid washed LCA CPG (loading = 115.2 μmol/g) were added to the main reaction mixture, vortexed shortly and placed on shaker for approximately 20 hours. Removed from shaker after 20 hours and the loading was checked. A small

sample of CPG was washed with copious amounts of acetonitrile, dichloromethane, and then with ether. The initial loading was found to be 49 $\mu\text{mol/g}$. (2.9 mg of CPG were cleaved with trichloroacetic acid). The absorption of released trityl cation was read at 503 nm on a spectrophotometer to determine the loading. The whole CPG sample was then washed as described above and dried under P_2O_5 overnight in vacuum oven. The following day, the CPG was capped with 50 mL CAP A (tetrahydrofuran/acetic anhydride) and 50 mL CAP B (tetrahydrofuran/pyridine/1-methyl imidazole) for approximately 1 hour on the shaker. The material was filtered and washed with dichloromethane and ether. The CPG was dried under P_2O_5 overnight in vacuum oven. After drying, 33.00 g of CPG was obtained with a final loading of 66 $\mu\text{mol/g}$.

EXAMPLE 15

5'-O-DMT-3'-O-(2-methoxyethyl)-N²-isobutyryl-guanosine-2'-O-succinate

[0150] 5'-O-DMT-3'-O-(2-methoxyethyl)-N²-isobutyryl guanosine was succinylated on the 2'-sugar position. 3.0 g (4.20 mmol) of the guanosine nucleoside were reacted with 10.5 mL dichloroethane, 631 mg (6.30 mmol) succinic anhydride, 585 μL (4.20 mmol) triethylamine, and 257 mg (2.10 mmol) 4-dimethylaminopyridine. The reactants were vortexed until dissolved and placed in heating block at 55 °C for approximately 30 minutes. Completeness of reaction checked by thin layer chromatography (TLC). The reaction mixture was washed three times with cold 10% citric acid followed by three washes with water. The organic phase was removed and dried under sodium sulfate. The succinylated nucleoside was dried under P_2O_5 overnight in vacuum oven.